Current Imaging Strategies of Primary and Secondary Neoplasms of the Liver

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ABSTRACT

This article details the diagnosis and imaging of primary and secondary neoplasms of the liver. Benign conditions that can mimic malignancy are also discussed, such as focal nodular hyperplasia and adenoma. Considerable attention is given to hepatoma, which is the most common primary hepatic tumor in the United States. The roles of magnetic resonance imaging, computed tomography, and ultrasound are evaluated, with recommendations for their effective use. Pitfalls in imaging related to posttreatment changes and unusual patterns of metastatic disease are illustrated.

KEYWORDS: Cancer, liver, hepatoma, imaging, metastasis

Objectives: Upon completion of this article, the reader should (1) know the primary hepatic neoplasms and the major benign conditions that can mimic malignancy, and (2) understand the uses of ultrasound, computed tomography, and magnetic resonance imaging in diagnosing hepatic tumors.

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PRIMARY LIVER MALIGNANCIES

Hepatoma

The most common malignant primary liver tumor in U.S. adults is hepatocellular carcinoma (HCC) or hepatoma, which arises from hepatocytes.¹ This represents ~70 to 80% of all primary liver tumors. In the western world, up to 75% of the people who develop hepatoma also have cirrhosis. Still, hepatoma is a relatively uncommon tumor in the United States, comprising only ~2% of all reported malignancies. In the rest of the world it is more common and is the third leading cause of cancer-related mortality. In the United States, HCC is more common in men than women and

is typically seen in older patients with cirrhosis.^{2,3} Infection with either hepatitis B or hepatitis C is associated with an increased risk of cirrhosis and liver cancer. Chronic hepatitis B carriers have a 100-fold higher risk of developing HCC than the general population. In one study in Taiwan, hepatitis B virus surface antigen (HBsAg) chronic carriers had a risk of HCC 217 times that of a noncarrier.⁴ In the same study, 51% of deaths of HBsAg carriers were caused by liver cirrhosis or HCC as compared with 2% of the general population.

Hepatitis B is a DNA tumor virus. The oncogenic mechanism is incorporation of viral DNA into the host genome of infected hepatocytes by reverse

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transcription, leading to malignant transformation. This may explain the frequent multicentric nature of the tumor. Coinfection with hepatitis D has been shown to increase the risk of chronic liver disease to 70 to 80%, as compared with a rate of 15 to 30% in patients who are only infected by hepatitis B.⁵ The rate of hepatitis B–associated hepatoma is decreasing slowly in the United States due to the availability of an effective vaccine.⁶

Chronic hepatitis C infection has also been recognized as an important risk factor for the development of HCC. Hepatitis C is a single-stranded flaviviridae RNA virus that is not incorporated into the host genome. The mechanism of carcinogenesis may be indirect, due to chronic inflammation. Hepatitis C was first recognized in the U.S. population in the 1960s, related to blood transfusion and injected drug use. The first reliable serological test became available in the early 1990s. Studies indicate that in chronic hepatitis C virus infection, the lifetime risk of cirrhosis is 20 to 50%, with the resultant increased risk of hepatoma. The mean duration between infection and the first diagnosis of cirrhosis is ~20 years. It is estimated that at least 200 million people worldwide are infected with hepatitis C virus, with ~1% of these in the United States. The incidence of infection is increasing both in the world and U.S. populations; hepatitis C is now the most common cause of cirrhosis in the United States. Hepatitis C accounts for 20% of acute hepatitis and 70% of chronic hepatitis and is present in 40% of cases of end-stage cirrhosis seen in the western world.⁷

Rare conditions that cause cirrhosis, such as hemochromatosis, Wilson's disease, and sclerosing cholangitis, are also associated with a high incidence of hepatoma. In Asia and Africa, aflatoxin found in moldy peanuts and grain is an important cause of this malignancy. This byproduct of fungal contamination causes DNA damage with p53 mutation. In parts of Africa, hepatoma is the most common cancer. Hepatomas in these regions often occur in children or young adults without cirrhosis.⁸

DIAGNOSIS

Physical examination is usually not helpful. As most hepatomas occur in the setting of cirrhosis, any progression of hepatic failure could be due to the preexisting condition. The presence of ascites may make palpation of the liver for a focal enlarging mass impossible. Hepatic encephalopathy can complicate history taking. Alpha-fetoprotein (AFP) is the most important nonimaging diagnostic tool. AFP is elevated in only a few malignancies, mainly germ cell tumors and hepatomas,⁹ and ~75% of HCCs show an elevated AFP level. The normal level in adult humans is 5 to 10 ng/mL, but chronically elevated levels of up to 30 ng/mL have been

found in certain families.¹⁰ An elevation of greater than 400 ng/mL predicts HCC with a specificity of greater than 95%. In the setting of preexisting cirrhosis, AFP levels are often obtained serially. A rising level above 100 ng/mL is frequently the cutoff for more invasive screening procedures.¹¹

RADIOLOGICAL SCREENING

Hepatomas are usually hypervascular and derive their blood supply from the hepatic artery. A good arterial contrast bolus and proper imaging time are critical. This is useful in distinguishing focal nodular hyperplasia (FNH) or regenerating nodules from tumor, as benign conditions are mainly perfused by the portal vein. Although solitary nodules are possible, hepatomas in cirrhotics are frequently multifocal. A central mass with satellite nodules adjacent to it is a common pattern. Portal vein thrombosis extending from the tumor mass is another distinguishing sign (Fig. 1); this finding is rarely seen in metastasis or other primary liver tumors. In advanced cases, tumor may spread beyond the liver capsule with the development of peritoneal seeding. The omentum, paracolic gutters, and subphrenic recesses should be carefully screened in any patient with ascites and an exophytic tumor. Biliary obstruction is uncommon except in mixed cholangiocarcinoma/hepatoma-type tumors. Distant lung metastases are frequently seen in advanced disease.

In the setting of a rising AFP level, ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) may be performed. As early stage disease can be treated by resection or liver transplantation, serial 6-month follow-up imaging studies may be justified in some patients with long-standing cirrhosis. It is important to examine the entire liver for lesions as hepatomas are often multicentric.

Ultrasound remains highly operator-dependent but is the least expensive imaging method. Doppler assessment should be done to evaluate the flow in the portal vein, as vascular invasion is common in advanced

Figure 1 Contrasted CT showing an advanced left hepatoma with typical portal venous invasion.

hepatoma. CT is a common imaging modality for hepatoma screening.¹² A triphasic technique including noncontrast, arterial (early), and portal venous (late) imaging is recommended. It is tempting to eliminate the noncontrast portion of the study, but frequently venous access may be impaired (e.g., intravenous drug user with portal hypertension due to cirrhosis) and the contrasted phases may be closer to equilibrium. Retrograde (hepatofugal) flow can also impair contrasted CT evaluation. Thinner sections through the liver serve to eliminate volume averaging, and given modern spiral technology, 5-mm sections should be obtained with the option for thinner reconstruction. This helps eliminate confusion with biliary cysts, which can contain high-attenuation bilious fluid but have a sharply defined wall without enhancement. A total of 100 to 150 mL of nonionic contrast, injected at a rate of at least a 2 mL/s, is needed to take full advantage of the ability of CT to access neovascularity. Hepatomas are usually hypervascular tumors with the highest conspicuity in the arterial phase; the presence of neovascularity helps to differentiate them from benign conditions such as adenomas or hemangiomas.

MRI is increasingly used for hepatoma screening. Noncontrasted T1- and T2-weighted hepatic evaluation is done to assess the structural anatomy and parenchymal edema. Currently the most sensitive method for hepatoma detection involves dynamic contrast imaging with a T1-weighted breath-hold gradient technique. Paramagnetic extracellular contrast agents containing gadolinium remain the agents of choice. Gadolinium-containing compounds such as Magnevist® (Berlex, Inc., Montville, NJ) are vascular agents similar in effect to CT contrast. They rapidly distribute in the vascular and interstitial spaces but do not cross cell membranes, with distribution therefore reflecting the perfusion pattern.

Other agents with preferential hepatocyte uptake have been evaluated. One class of compounds increases the signal of normal liver on T1-weighted images by hepatocyte uptake. These compounds include the water-soluble paramagnetic chelates MN-DPDP (Mangafodipyr®; Amersham Health, Little Chalfont, Buckinghamshire, United Kingdom), Gd-BOPTA (Amersham Health), and Gd-EOB-DTPA (Eovist®; Amersham Health).¹³ A second approach is to use superparamagnetic iron oxide particles that improve conspicuity by uptake in the reticuloendothelial (RES) cells, darkening the normal parenchyma by T2 relaxation. Hepatomas either do not contain RES cells or have markedly decreased activity of these cells, thereby increasing the visualization of tumors against the dark background of normal liver tissue. These compounds include AMI-25 (Feridex®; Berlex, Inc.) and SH U 555A (Resovist®; Amersham Health).¹⁴ Unfortunately, contrast uptake by hepatocellular carcinoma can be observed with these two

classes of agents. Special considerations for patients undergoing MRI include claustrophobia, patient cooperation with breath-hold techniques, and the interference of ascites. MRI is less useful for extrahepatic evaluation than CT but may have a slightly higher conspicuity for parenchymal lesions and vascular invasion. With renal failure or known CT contrast allergy, MRI is extremely useful in identifying potential sites of tumor. Given recent concerns with repeated radiation exposure in CT screening, MRI is also a viable alternative for the cirrhotic patient who may need repeated screening studies.

STAGING

The staging of hepatocellular carcinoma is somewhat controversial. The standard tumor, node, metastasis (TNM) approach of the American Joint Committee on Cancer (AJCC) does not take into account clinical factors that have importance in prognosis. Recently, numerous other staging systems have appeared, including The Cancer of the Liver Italian Program (CLIP),¹⁵ the Japan Integrated Staging (JIS),¹⁶ and the Barcelona Clinic Liver Cancer (BCLC) staging classifications.¹⁷ These include integration of clinical information usually not available to radiology, but they have better correlation with prognosis than that usually seen in the TNM classifications.

TNM staging follows the standard format for most malignancies¹⁸ (Table 1). During 2002, the tumor size criteria of the AJCC changed from 2 cm to 5 cm. A T1 malignancy is a solitary mass without vascular invasion. Multiple tumors of 5 cm or less without vascular invasion, or a single tumor with vascular invasion, are staged as T2. T3 lesions are multiple tumors greater than 5 cm in size or a single tumor involving a major branch of the portal or hepatic veins. T4 lesions involve perforation of the visceral peritoneum or extension to organs other than the gallbladder. Nodal staging is N1 if the regional lymph nodes such as the hilar, hepatoduodenal, or periportal are affected. The hiatal, periaortic, and subdiaphragmatic nodes are considered distant metastasis. The presence of distant metastasis is graded as M1.

Table 1 AJCC Hepatoma Stage Groupings

Stage 1: T1, N0, M0
Stage 2: T2, N0, M0
Stage 3a: T3, N0, M0
Stage 3b: T4, N0, M0
Stage 3c: Any T, N1, M0
Stage 4: Any T, any N, M1

T1, solitary mass without vascular invasion; T2, multiple tumors, all 5 cm or less, without vascular invasion or a single tumor with vascular invasion; T3, multiple tumors > 5 cm in size or a single tumor involving a major branch of the portal or hepatic veins; T4, perforation of visceral peritoneum or extension to organs other than the gallbladder; N1, involvement of the regional (hilar, hepatoduodenal, periportal) lymph nodes; M1, distant metastasis.

Stages 1 through some stage 3b are considered localized and potentially resectable for cure. Any radiological attempt at staging should include the maximum diameter of the tumor or tumors, the specific segmental location and number of lesions, any evidence of vascular invasion, nodal enlargement, or distant metastases. Any vascular variants that could affect resection should be noted as well.

Fibrolamellar Hepatic Cancer

This is a distinct variant of HCC with malignant hepatocytes enmeshed in lamellar fibrous tissue. Fibrolamellar cancer of the liver occurs in children or young adults with a female predominance. The average age range at presentation is 20 to 40 years of age. It is not associated with cirrhosis or hepatitis, and AFP is rarely elevated. There is a survival advantage when compared with classic hepatomas.^{19,20}

In contrast to most hepatomas, these tumors present as solitary nodules in a noncirrhotic liver. They are less vascular than other hepatomas and may show a more organized structure on imaging evaluation. A central stellate scar may be present. This scar usually does not enhance and is hypointense on T1- and T2-weighted MRI.²¹ MRI will demonstrate the central scar if present and may show a pseudocapsule²² (Fig. 2). By contrast, the stellate scars of focal nodular hyperplasia or atypical hemangiomas are vascular and will often show some enhancement on arterial phase imaging, with fill in on delayed studies. There is an overlap in appearance with FNH, and it has been suggested that FNH may be a precursor lesion. Ultrasound shows a solitary well-defined mass with mixed echotexture. The central scar appears as a hyperechogenic structure but is seen in only half as many patients as in CT imaging. Tumor in lymph nodes, both by ultrasound and CT, may show similar central defects, thought to represent areas of tumor necrosis.

Figure 2 T2-weighted MRI of a fibrolamellar hepatoma. Note the central low-signal scar and the pseudocapsule.

Cholangiocarcinoma

Cholangiocarcinomas are cancers of the biliary duct system, extending from the liver to the ampulla of Vater in the pancreatic head. Tumors are classified into three distinct anatomic regions: intrahepatic, extrahepatic/perihilar, and distal extrahepatic. The perihilar (Klatskin) tumors are the most common and occur at the bifurcation of the right and left hepatic ducts. Purely intrahepatic tumors are the least common. More than 90% of all cholangiocarcinomas are adenocarcinomas, with the remaining tumors being squamous malignancies.²³

Risk factors for cholangiocarcinoma involve chronic inflammation. Primary sclerosing cholangitis (PSC) and parasitic infections are associated with increased risk. Congenital abnormalities such as choledochal cysts and Caroli disease have also been associated with cholangiocarcinoma. Some chemical agents, such as thorotrast, have also been associated.²⁴ Unlike hepatoma, cirrhosis and hepatitis do not increase risk. A strong association is seen in patients with both ulcerative colitis and PSC, with a lifetime risk of developing cholangiocarcinoma of 10 to 20%. About 2500 new cases occur in the United States every year as compared with 5000 cases of gallbladder cancer and 15,000 cases of hepatocellular cancer. Clinical symptoms are related to biliary obstruction and include jaundice, pruritus, clay-colored stools, and dark urine.²⁵

Radiological imaging involves assessment of the ductal anatomy. Ultrasound is often the first test used to evaluate a jaundiced patient. Ductal dilatation is easy to visualize, but the actual obstructing mass may be small. It is important to check for extraluminal extension of any obstructing process, as this suggests tumor (Fig. 3). Masses near the ampulla are often obscured by gas

Figure 3 Multicentric cholangiocarcinoma by contrasted CT. There is increased soft tissue around the portal triads with parenchymal invasion. Mild biliary obstruction is present. Note the central stent.

Figure 4 Gallbladder variant of cholangiocarcinoma demonstrating both the characteristic cauliflower appearance and delayed intense neovascular CT contrast enhancement.

during ultrasound imaging; CT scanning is useful in these cases.

CT imaging study should be performed with both oral and intravenous contrast. Image thickness should be 5 mm or less. It is helpful to give the patient additional oral contrast just before scanning to ensure that the duodenum is well filled. Occasionally, duodenal diverticula can be large and may mimic enlarged ducts or lymph nodes. Cholangiocarcinomas may show prolonged and intense contrast enhancement (Fig. 4).

MRI cholangiography is useful in visualizing the biliary anatomy noninvasively.^{26,27} Both thick-slab angled coronal T2 fast gradients and thin-section (3 mm) axial T2 gradient imaging is useful. When a cholangiocarcinoma is suspected, additional imaging sequences through the liver to check for parenchymal spread and multicentric lesions are necessary. Tumors typically demonstrate gadolinium enhancement. Given the limited time an MRI cholangiography protocol takes, it is not unreasonable to add a full liver assessment. MRI cholangiography may be impossible to perform in the presence of large-volume ascites or dilated bowel, due to the fluid interfering with signal arising from the ductal fluid.

Gallbladder Carcinoma

Gallbladder carcinoma is relatively rare in the United States, with a reported incidence of fewer than 5000 new cases each year. The mortality is high, as most cases are advanced with local hepatic invasion at the time of diagnosis.²⁸ It is associated with gallstones in 80 to 90% of cases, and there is a higher risk with porcelain gallbladder, possibly due to the effects of chronic inflammation.²⁹ A characteristic cauliflower appearance with hypervascularity is often seen in on CT when scanning advanced primary malignancy with liver invasion. The most common metastasis to the gallbladder is

melanoma, accounting for ~75% of cases.³⁰ Melanoma metastases are submucosal and may appear as friable polyploid masses that eventually erode into the adjacent liver.

Sarcoma

There are a range of sarcoma variants that primarily involve the liver, including angiosarcoma, malignant mesenchymoma, teratosarcoma, and rhabdomyosarcoma.³¹ These malignancies frequently present in childhood. In adults, angiosarcoma has an association with industrial exposure to vinyl chloride and has also been associated with thorotrast exposure.^{32,33} On imaging studies, they usually present as solitary masses with abnormal vascularity and have been reported to cause high-output heart failure. Sarcomas may be difficult to distinguish from fibrolamellar tumors but usually lack a central stellate scar on cross-sectional imaging studies.³⁴

Hepatoblastoma

This is mainly a tumor of childhood that often presents under the age of 3 years. There is a slight male predominance.³⁵ It is associated with Beckwith-Wiedemann syndrome and hemihypertrophy.³⁶ Imaging studies demonstrate a large solitary hypervascular mass, often located in the right lobe of the liver.³⁷ Cystic change or calcification may be present. Hepatoblastoma is typically centrally echogenic on ultrasound and enhances on CT evaluation. MRI also can delineate the extent of disease but may require sedation in the young infant or child.

BENIGN LIVER TUMORS THAT CAN MIMIC NEOPLASMS

Hemangiomas

Hemangiomas are the most common benign liver tumors. They are vascular malformations that are mesenchymal in origin. Other mesenchymal tumors include hemangioendothelioma, hamartoma, or rarely teratoma. The U.S. incidence rate reported clinically is 2%; however, higher rates are noted at autopsy (up to 7%). The lesion is usually asymptomatic, although individual hemangiomas may rupture and bleed.³⁸ There is no association between cutaneous and hepatic hemangiomas. Several clinical syndromes are associated with hepatic hemangiomas, including von Hippel-Lindau (also renal and retinal angiomas), Kasabach-Merritt (giant hepatic hemangiomas), Riley-Smith syndrome (multiple hemangiomas with macrocephaly), and Klippel-Treanunay-Weber (multiple hemangiomas with hemihypertrophy). Multiple pregnancies, oral contraceptives, and steroid use have also been considered risk factors. Lesion size may range from

Figure 5 Large hemangioma with the typical early CT contrast pattern of prominent peripheral sinusoids.

less than a centimeter to, in the case of giant cavernous hemangiomas, over 20 cm.³⁹ The most characteristic location is in the right posterior hepatic lobe adjacent to the diaphragm.

Nuclear medicine, ultrasound, CT, MRI, and angiography have been used in the evaluation of hemangiomas. Tc99m sulfur colloid SPECT (single photon emission computed tomography) imaging of the liver coupled with Tc99m tagged red blood cells (RBCs) has been useful in distinguishing lesions ≥ 2 cm in size.⁴⁰ The parenchymal "holes" noted on sulfur colloid imaging will match with areas of hyperactivity on tagged RBC scans. Other lesions that are less vascular, such as metastasis, will not demonstrate such hyperactivity on RBC scans. Ultrasound may show hemangiomas as uniform echogenic lesions, likely due to the fine vascular structure of the lesions. Contrast-enhanced CT scans demonstrate early phase peripheral enhancement, sometimes with one or more central vessels or sinusoids (Fig. 5). They should become completely isodense to normal parenchyma in delayed-phase imaging. Unfortunately, only ~60 to 70% of hemangiomas follow this classic CT pattern. In the larger lesions, there may be areas of persistent

poor flow or scarring from thrombosis that are difficult to distinguish from tumors.⁴¹

Distinguishing tumor from hemangiomas was one of the first clinical indications for body MRI. The original criteria of prolonged hyperintense T2 signal are still valid. More recently, vascular enhancement agents with fast T1-weighted techniques are used, similar to CT-contrasted imaging (early peripheral enhancement with delayed fill in following gadolinium administration). In the case of giant cavernous hemangiomas, multiple separate fluid-fluid levels may be visible.⁴² Rarely, angiography is done to confirm the absence of neovascularity and arterioportal shunting demonstrated by hepatomas.

Adenomas

Adenomas are benign tumors of the hepatocytes without bile duct formation. They have a strong association with the use of oral contraceptives. A 25-fold increase in incidence is seen with contraceptive use for 9 or more years. Most tumors are solitary, but up to 20% of patients have multiple lesions. There is a strong female predominance, with 90% of the symptomatic patients being women. Anabolic steroid use also increases risk.⁴³

Adenomas are prone to central necrosis and bleeding in up to 50 to 60% of patients.⁴⁴ They lack a developed portal blood supply and are mainly perfused by the hepatic artery. Most lesions are subcapsular and a few are pedunculated. Malignant transformation can occur but is rare, with a less than 1% lifetime risk. The main differential diagnosis is with a well-differentiated hepatoma. The multiple lesions of liver adenomatosis have a higher rate of malignant progression and are not steroid-dependent.⁴⁵

Adenomas frequently appear as a solitary well-demarcated mass. Some demonstrate central areas of hemorrhage (Fig. 6A). By ultrasound, these tumors are hypoechoic and subcapsular.⁴⁶ With Doppler interrogation, there may be increased flow. CT demonstrates a

Figure 6 (A) Noncontrast CT of an actively bleeding pedunculated left-sided adenoma. (B) The T1-weighted corresponding image of the same adenoma showing extensive displacement without invasion of the parenchyma and vessels.

mass that is frequently encapsulated and may have central calcification. Without contrast, they are of low attenuation; however, there is a centripetal pattern of arterial phase enhancement that fills in on delayed imaging. Adenopathy suggests malignant degeneration or hepatoma. The MRI appearance is also variable. A subcapsular hemosiderin ring is suggestive of adenoma. Hyperintensity relative to normal liver may be seen on both T1- and T2-weighted lesions, which is felt to be due to the presence of fat. In one series, hyperintensity was present in 77% of adenomas for T1 sequences and 74% for T2 imaging.⁴⁷ MRI contrast, aside from gadolinium, is of limited usefulness. The presence of acute or subacute hemorrhage may make these lesions seem more irregular and aggressive, mimicking malignant lesions (Fig. 6B). Angiography will show a well-defined, rounded, hypervascular mass fed by numerous peripheral hepatic artery branches. There are tortuous enlarged vessels with flow moving centrally; avascular areas due to necrosis may be present.

Focal Nodular Hyperplasia

Focal nodular hyperplasia is a localized hamartoma that may resemble macronodular cirrhosis or fibrolamellar cancer.⁴⁸ It may be estrogen-sensitive and is normally seen in young premenopausal women. This tumor has also been called focal nodular cirrhosis or parenchymal hamartoma. It is usually solitary (80% of the time) and subcapsular and is rarely pedunculated.⁴⁹ Fibrous bands can radiate from a central stellate scar like fibrolamellar cancer. Unlike fibrolamellar hepatoma, the liver tissue between the bands is relatively normal, containing Kupffer cells, hepatocytes, and biliary ducts.⁵⁰ On imaging, the lesions may have a spoke-wheel pattern of contrast enhancement but do not demonstrate neovascularity.⁵¹ Because normal Kupffer cells are present, these tumors may demonstrate a normal uptake of Tc99m sulfur colloid on liver-spleen scans.

Hepatic Cysts

Cysts are usually asymptomatic and come to attention during imaging procedures for other causes.⁵² Polycystic disease may be associated with multiple and enlarging cysts in adults. True benign cysts should be anechoic on ultrasound, with thin walls and increased through transmission. These findings are very operator-dependent and are related to acoustic window limitations. With CT imaging, there should be no wall enhancement; the presence of an enhancing rim must raise the question of the rare cystic neoplasm. Volume averaging is a problem with lesions less than 1 cm in diameter, and the use of thinner CT sections (5 mm or less) is helpful. Although cysts have high conspicuity even on noncon-

trast scans due to the difference in density with normal liver parenchyma, contrast is necessary to evaluate for neovascularity. MRI is useful in cases of iodinated contrast allergy or renal failure. Fluid signal on T2-weighted image sequences is easy to assess. Frequently, additional lesions are found on MRI when compared with CT imaging. T1 breath-hold techniques with gadolinium are useful for vascular assessment.⁵³

METASTATIC LIVER CANCER

Metastatic cancer to the liver is by far the most common hepatic malignancy in the United States. Hematogenous metastasis from virtually any tumor can spread to the liver. The most common primary sources mimic the incidence of common neoplasms, with lung, breast, and colon being the most common. As the presence of hepatic spread usually indicates advanced and often incurable disease, the diagnosis of liver metastases is critical to accurate staging and prognosis. With the large physiological reserve of the liver, abnormalities in liver function tests appear late in the clinical course. Jaundice is usually late or relatively mild as the central biliary system is often spared from obstruction by peripheral hematogenously spread tumors.

Ultrasound, CT, and MRI are all commonly used in the evaluation of liver malignancies. There is a large variance in the appearance of metastatic disease. In general, metastases appear similar to the gross morphology of the primary tumor. Hypervascular tumors, such as renal cell carcinoma, frequently have hypervascular metastasis. Cystic primary neoplasms have cystic metastases; tumors with calcifications may also calcify in the liver. Ultrasound with microbubble enhancement may allow identification of small lesions not well imaged by CT or MRI.⁵⁴ CT angiography/portography is a specialized method of hepatic assessment performed in certain centers when a high sensitivity to any potential liver defect is important.⁵⁵ This technique takes advantage of the fact that the tumor vascular supply is derived from the hepatic arterial circulation; normal liver parenchyma is preferentially perfused by the portal vein. This technique has exquisite sensitivity to perfusion abnormalities but is of low specificity. Still, if resection of metastatic lesions is being considered, this is an excellent method of fully staging any potential tumor burden prior to surgery.⁵⁶

UNUSUAL PATTERNS OF MALIGNANCY WITH PITFALLS IN IMAGING

Certain tumor patterns are associated with specific malignancies. Melanoma preferentially spreads along the visceral surface of the liver and may spontaneously bleed. Cystadenocarcinomas often present as cystic lesions in the liver. Lymphoma is usually diffuse with

Figure 7 Lipiodol appearing as high-density material on a non-contrasted CT postchemoembolization.

hepatomegaly but may present as nodular masses. Colon carcinoma of the hepatic flexure may directly invade the liver with abscess formation. As tumors of the right hemicolon rarely obstruct, they may reach a very large size and present as a palpable right upper quadrant mass. If they rupture into the liver, the clinical presentation may include sepsis and mimic hepatic abscess. Oral contrast visualized in the lesion on CT imaging should suggest this possibility.

Posttreatment changes on imaging studies are becoming increasingly common as patients survive longer due to more effective cancer treatments. Treated metastasis may regress, leaving areas of scarring, retraction, and calcification. Following chemotherapy, diffuse fatty infiltration may develop in the liver; sometimes this focally spares the segments involved with tumor. Postresection hypertrophy of the remaining liver is normal and may mimic recurrent tumor. Vascularity should be normal, but the contour of the remaining liver, particularly with extended hepatectomies, is often markedly abnormal and masslike. Postoperative baseline studies are useful. Portal thrombosis

Figure 8 Liposarcoma on contrasted CT mimicking a primary hepatic tumor. Note the hepatic and renal displacement, which localizes this tumor outside of the liver.

is usually specific to hepatoma but may be rarely seen in other tumors, such as renal cell metastasis or the occasional colon tumor. Long-standing cirrhosis, including that resulting from congenital portal atresia, may have a nodular appearance that mimics hepatoma. Correlation with serum AFP levels is useful. Lipiodol, as part of a chemoembolization protocol, will be visualized as high-density material in the embolized liver (Fig. 7). This oil-soluble agent may be persistent for years following treatment and can be useful to follow areas of potential tumor recurrence. Angiography to identify tumor vasculature may be necessary in certain cases. Large extrahepatic masses, especially renal or adrenal tumors, may directly invade the liver. As these are hypervascular, they may mimic advanced hepatoma (Fig. 8). Careful attention to the vasculature and the center point of malignancy will frequently allow differentiation of external tumor extension from a tumor arising in the liver.

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